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Remarks

I. Status of the Claims and Amendments to the Specification

Amendments to the specification are sought to correct minor typographical errors, to add reference to SEQ ID NOs and to insert a Substitute Sequence Listing, submitted herewith. In accordance with 37 C.F.R. § 1.825(a), this submission includes no new matter. In accordance with 37 C.F.R. § 1.825(b), the paper copy of the Sequence Listing and the computer readable copy of the Sequence Listing submitted herewith in the above-captioned application are the same. Accordingly, the foregoing amendments to the specification do not introduce new matter, and their entry is respectfully requested.

Upon entry of the foregoing amendments; claims 1-102, 104, 108, 122-132, 134-137, 139, 140-174, 176-179, 185-189 and 194-218 are pending in the application, with claims 1, 87, 100, 135, 165, 177 and 187 being the independent claims. Claims 5, 103, 105-107, 109-120, 133, 138, 175, 180-184 and 190-193 are sought to be cancelled without prejudice to or disclaimer of the subject matter therein. Claims 12, 36-42, 50-85, 87-99, 157-172, 194-197 and 199-218 are withdrawn from consideration. Amendment is sought to claims 1, 6-8, 14, 19, 21, 22, 33, 35, 47, 49, 86, 100, 104, 108, 121-126, 130, 132, 134, 135, 139, 140-144, 152, 154, 155, 176, 177, 187 and 198. Claim 219 is new. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Claim 1 has been amended to incorporate the elements of dependent claim 5, and to recite that "said first attachment site does not comprise a sulfhydryl group". Claims 6 and 7 have been amended to remove reference to cancelled claim 5, and to properly depend from amended claim 1. Claim 100 has been amended to incorporate elements of dependent claims 103, 105 and 121. Claim 135 has been amended to incorporate elements of claims 155 and 156, which originally depended from claim 135. Following the amendment to claim 135, claims 155 to 164 have been amended to depend directly, or ultimately, from claim 1. Hence

the above-noted amendments to claims 1, 6, 7, 100 and 135 are fully supported by the claims as originally filed.

Support for the amendment to claim 135, wherein the claimed antigen or antigenic determinant is VEGFR-II or a peptide or fragment thereof, is found in the specification at, *inter alia*, Figures 10 and 18, and pages 13, 56, 129-135, and 190-194.

The subject matter of claims 133 and 134 have been combined into amended claim 134, with cancellation of claim 133.

Two versions of claim 152 were originally filed. Accordingly, the first version of claim 152 has been deleted and is now presented as new claim 219, containing identical subject matter but depending from claim 151.

Claim 176 has been amended to depend from any one of claims 1, 87, 100, 135 or 165, rather than claim 160.

To comply with 37 C.F.R. §§ 1.821-1.825 claims 33, 42, 49, 86, 132 and 159 have been amended to add reference to SEQ ID NOs. In accordance with 37 C.F.R. § 1.825(a), this amendment includes no new matter.

Claims 1, 14, 19, 21, 22, 35, 39, 40, 47, 98, 100, 108, 122-125, 130, 134-135, 139, 140, 141, 142-144, 152, 176, 177 and 187 have been amended to correct minor typographical errors, and/or to place these claims into better form for U.S. practice.

Accordingly, the foregoing amendments to the specification and claims introduce no new matter, and their entry and consideration, and reconsideration of the present application, are respectfully requested.

II. Summary of the Office Action

In the Office Action dated March 1, 2004, the Examiner objected to the specification and claims for failure to conform to 37 C.F.R. §§ 1.821-1.825; claims 12, 36-42, 50-85, 87-99, 106, 107, 109-120, 157-172, 180-184, 190-197 and 199-218 were withdrawn from consideration; claims 2-11, 13-35, 43-49, 86, 101-105, 108, 121-134, 136-156, 173, 174, 177-179, 185-189 and 198 were objected to; claims 1, 100, 175 and 176 were rejected under 35 U.S.C. § 112; claims 1 and 135 were rejected under 35 U.S.C. § 102(b); claim 100 was rejected under 35 U.S.C. § 102(e); and claim 100 was rejected under 35 U.S.C. § 103(a). Applicants respectfully offer the following remarks concerning each of these elements of the Office Action.

III. Objection to the Specification

On page 3 of the Office Action the Examiner objected to the specification for failure to fully comply with 37 C.F.R. §§ 1.821-1.825. Accordingly, Applicants have amended the specification and claims and provided a substitute Sequence Listing. Applicants believe that the specification, claims and Sequence Listing fully comply with 37 C.F.R. §§ 1.821-1.825. Therefore, this objection has been overcome. Reconsideration and withdrawal of the objection are respectfully requested.

IV. Objection to the Claims

The Examiner objected to claims 1-11, 13-35, 43-49, 86, 100-105, 108, 121-156, 173-185 and 198 as allegedly not being limited to the elected invention (Office Action at 2). Applicants respectfully traverse this objection.

> Where the requirement for restriction in an application is predicated upon the nonallowability of generic or other type of linking claims, applicant is entitled to retain in the case claims to the nonelected invention or inventions.

> If a linking claim is allowed, the examiner must thereafter examine species if the linking claim is generic thereto, or he or she must examine the claims to the nonelected inventions that are linked to the elected invention by such allowed linking claim.

MPEP § 809.04. Applicants respectfully request that this objection be held in abeyance pending the identification of allowable subject matter, at which time rejoinder of species linked by an allowable generic claim will be proper under MPEP § 809.04.

V. Rejections Under 35 U.S.C. § 112, Second Paragraph

In the Office Action at page 4, the Examiner rejected claim 1 and 135 under 35 U.S.C. § 112, second paragraph, alleging that the term "virus-like particle of a bacteriophage" is unclear (Office Action at 4).

Applicants respectfully disagree and traverse this portion of the rejection. The phase to which the Examiner objects has been specifically defined:

> Virus-like particle of a bacteriophage: As used herein, the term "virus-like particle of a bacteriophage" refers to a virus-like particle resembling the structure of a bacteriophage, being non replicative and noninfectious, and lacking at least the gene or genes encoding for the replication machinery of the bacteriophage, and typically also lacking the gene or genes encoding the protein or proteins responsible for viral attachment to or entry into the host. This definition should, however, also encompass virus-like particles of bacteriophages, in which the aforementioned gene or genes are still present but inactive, and, therefore, also leading to non-replicative and noninfectious virus-like particles of a bacteriophage.

Specification at 23. Thus, the term "virus-like particle of a bacteriophage" as used in claim 1 would be readily understood by one of ordinary skill, based on the explicit definition of this term in the present specification. Accordingly, this portion of the rejection is in error and should be withdrawn.

The Examiner next rejected claim 100 under 35 U.S.C. § 112, alleging that the term "self antigen" is unclear, because any antigen which is "self" to one organism is non-self to

another. Applicants respectfully disagree, and traverse this portion of the rejection. The phase to which the Examiner objects has been specifically defined:

> Self antigen : As used herein, the tem "self antigen" refers to proteins encoded by the host's DNA and products generated by proteins or RNA encoded by the host's DNA are defined as self. In addition, proteins that result from a combination of two or several self-molecules or that represent a fraction of a self-molecule and proteins that have a high homology to self-molecules as defined above (>95%)may also be considered self.

Specification at 22. The concept of self antigen is understood in the context of self-tolerance, which is taught in the specification at, for example, page 92: "The immune system usually fails to produce antibodies against self-derived structures . . . due to tolerance." Furthermore, the term "self-antigen" is well understood in the art. For example, page 592 of the Oxford Dictionary of Biochemistry and Molecular Biology (1997) defines self antigen as "any (potentially) antigenic molecule originating in an individual that is recognized as nonforeign by the individual's immune system, and to which immunological tolerance is normally shown."

While the term "self antigen" may be relative to a particular organism, this does not render the term indefinite. An animal will, normally, tolerate any potential antigen produced from its own genome and any potential antigen that, although not produced from their own genome, is sufficiently antigenically related to a potential antigen that *is* produced from its own genome such that self-tolerance is not overcome. By contrast, an animal will not normally be tolerant to non-self antigens, including viral, bacterial or pathogen-associated antigens. Hence, "self antigen" is a well understood term of art that encompasses a range of antigens, and excludes other antigens. Additionally, Applicants have provided numerous non-limiting examples of self antigens in the present specification.

As the Board has held:

> [35 U.S.C. § 112, second paragraph] merely requires that the claims set forth and circumscribe a particular area with a reasonable degree of precision and particularity. The definiteness of the claim language employed must not be analyzed in a vacuum, but always in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one having ordinary skill in the pertinent art.

Ex parte Moelands, 3 USPQ2d 1474, 1476 (Bd. Pat. App. Int. 1987) (citing *In re Moore*, 439 F.2d 1232 (CCPA 1971). As discussed above, the term "self antigen" is routinely used in the art, and has been specifically defined in the present specification. In addition, this term is used throughout the present claims in a manner that is consistent with its usual meaning in the art and with its definition in the specification. Hence, Applicants respectfully contend that one of ordinary skill could easily determine the scope of the self antigens that are encompassed by claim 100 (and the other claims) as currently presented. The present claims thus comport with the requirements of 35 U.S.C. § 112, second paragraph, as interpreted under *Moelands* and *Moore*. Reconsideration and withdrawal of this portion of the rejection therefore are respectfully requested.

The Examiner has next rejected claim 176 for reciting "the vaccine composition of claim 160," alleging that claim 160 is not drawn to a vaccine. Claim 176 has been amended, accommodating this portion of the rejection.

Accordingly, the claims as currently presented specifically point out and distinctly claim the subject matter regarded by Applicants as the invention. Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

VI. Rejections Under 35 U.S.C. § 112, First Paragraph

In the Office Action at pages 4-5, the Examiner has rejected claims 175 and 176 under 35 U.S.C. § 112, first paragraph, alleging that the specification does not provide enablement for a vaccine composition. Applicants respectfully disagree, and traverse this rejection.

The Examiner bears the initial burden of proving that a specification is non-enabling. *See In re Marzocchi*, 169 USPQ 367 (C.C.P.A. 1971). It is axiomatic that a specification is presumed to be enabling unless the Examiner provides acceptable objective evidence or sound scientific reasoning showing that it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention. *See Id.*; *see also In re Wright*, 999 F.2d 1557, 1562 (Fed. Cir. 1993) ("Without a reason to doubt the truth of the statements made in the patent application, the application must be considered enabling."). Applicants assert that the Examiner has not demonstrated by sufficient objective evidence that the claimed embodiments are not enabled.

Further, in making these contentions, the Examiner contends that "the specification provides no evidence that immunization with the VEGFR-II particle will prevent disease, and it is not well established in the art that immunological methods are effective in prevention." (Office Action at 5). The Examiner appears to suggest that for the claimed invention to be enabled, Applicants must demonstrate the clinical efficacy of the claimed methods (*i.e.*, that the methods are without obstacles, are safe, and are therapeutically effective) in order to overcome the outstanding enablement rejection.

Applicants wish to remind the Examiner, however, that there is no requirement for clinical data to prove that an application is in compliance with 35 U.S.C. § 112, first paragraph. In fact, description of *in vitro* and/or animal testing has been held to enable claims to *in vivo* therapeutic compositions and methods of their use. To this end, the Federal Circuit has stated that:

> In vitro testing, in general, is relatively less complex, less time consuming, and less expensive than in vivo testing. Moreover, in vitro results with respect to the particular pharmacological activity are generally predictive of in vivo test results, i.e., there is a reasonable correlation therebetween. Were this not so, the testing procedures of the pharmaceutical industry would not be as they are.

Cross v. Iizuka, 753 F.2d 1040, 1050 (Fed. Cir. 1985); *see also In re Brana*, 51 F.3d 1560, 1567-68 (Fed. Cir. 1995) (holding that animal testing results are sufficient to establish whether one skilled in the art would believe that a pharmaceutical compound has an asserted clinical utility for the purposes of compliance with the enablement requirement of 35 U.S.C. § 112, first paragraph).

Furthermore, Applicants also note that MPEP § 2164 states:

> Since the initial burden is on the examiner to give reasons for the lack of enablement, the examiner must also give reasons for a conclusion of lack of correlation for an *in vitro* or *in vivo* animal model example. A rigorous or an invariable exact correlation is not required, as stated in *Cross v. Iizuka*, 753 F.2d 1040, 1050, 224 USPQ 739, 747 (Fed. Cir. 1985):
> [B]ased upon the relevant evidence as a whole, there is a reasonable correlation between the disclosed *in vitro* utility and an *in vivo* activity, and therefore a rigorous correlation is not necessary where the disclosure of pharmacological activity is reasonable based upon the probative evidence. (Citations omitted.)

Hence, Applicants are not required to demonstrate clinical efficacy to enable therapeutic claims, but are, rather, required merely to demonstrate that the claim is reasonable in scope based on the relevant evidence as a whole. Applicants have clearly met, and have indeed exceeded, this standard.

For example, the specification at pages 55-56 indicates that VEGF and VEGFR-II are important in vascularization of solid tumors and are recognized by those of ordinary skill in the art as important therapeutic targets for cancer. Inhibition of tumor growth in mice using sera specific for VEGFR-II has been demonstrated. (Wei, Y.Q., *et al.* (2000) Nature Medicine 6, 1160-1165; cited at page 56 of the specification; and provided as Document

AT129 in Applicants' Information Disclosure Statement, filed November 13, 2002). In Example 12 of the specification, Applicants constructed a VLP-VEGFR-II conjugate which was used to immunize mice. Strong antibody responses were observed in immunized mice. Example 49 also discloses a Qβ VLP-VEGFR-II peptide vaccine.

In addition, the specification also provides evidence for enablement of vaccines against additional antigens, self-antigens and allergens, including DerP1, Aβ, FLAG, VEGF, PLA_2, TNFα, and influenza, among others. For example, in Example 19 of the present specification, mice sensitized to PLA_2 that were vaccinated with PLA_2-Qβ conjugate did not show anaphylaxis on subsequent challenge with PLA_2, while unvaccinated control mice showed an anaphylactic response on PLA_2 challenge. In Example 40, Mice immunized with VLP conjugated to M2 protein of influenza were protected from subsequent viral challenge.

Under *Cross* and *Brana*, one of ordinary skill would thus recognize that the animal assays described in the present specification would be sufficient to support the asserted utility and that one would have a reasonable expectation that the claimed methods would be successful for the claimed *in vivo* therapeutic approaches.

Applicants also assert that one of ordinary skill in the art would not require undue experimentation to make or use the vaccine compositions of the presently claimed invention. Indeed, Applicants have already demonstrated vaccine efficacy in animals, thus fully enabling the claimed vaccine compositions. For at least the above reasons, Applicants respectfully contend that claim 176 fully complies with 35 U.S.C. § 112, first paragraph. Claim 175 is cancelled, and rendering moot the rejection of that claim. Reconsideration and withdrawal of the rejection is respectfully requested.

VII. Rejections Under 35 U.S.C. § 102

A. The rejection over Mastico et al.

In the Office Action at page 5, the Examiner has rejected claims 1 and 135 under 35 U.S.C. § 102(b) as allegedly being anticipated by Mastico *et al.*, U.S. Patent No. 5,698,424. Applicants respectfully traverse this rejection.

In order to expedite prosecution, and not in acquiescence to Examiner's rejection, Applicants have amended claim 1 to incorporate elements from dependant claims 5 and 22; and have amended claim 135 to incorporate elements from dependant claims 155 and 156. As claims 5, 22, 155 and 156 were not rejected over Mastico *et al.*, Applicants presume that the Examiner has determined that these claims are allowable over this reference. Since the subject matter of these claims has now been incorporated into claims 1 and 135, Applicants respectfully contend that claims 1 and 135 are now allowable.

Nevertheless, Mastico *et al.* do not disclose or suggest the presently claimed invention, but are limited to the disclosure of a peptide or an enzyme coupled to the surface of a modified MS-2 bacteriophage particle via the sulfhydryl group of one cysteine residue inserted within the coat protein of MS-2.

By contrast, the compositions of present claim 1 differ from those disclosed in Mastico *et al.* in that proteins, peptides or other antigens in the present composition are bound to the bacteriophage particle by means that do not involve a sulfhydryl group as attachment site on the part of the bacteriophage particle. Disadvantages associated with the use of sulfhydryl groups and cysteine residues, respectively, as attachment sites on the part of the bacteriophage for the association to antigens have been described within the present specification on page 47 second last and last paragraph. Accordingly, not only is the presently claimed invention distinguished from Mastico *et al.*, but show surprisingly superior properties over the compositions of Mastico *et al.* The compositions of present claim 135

also differ from those of Mastico *et al.* in that the reference does not disclose or suggest, inter alia, the use of VEGFR-II or peptide or fragments thereof.

Accordingly, Mastico *et al.* do not disclose the presently claimed invention, and hence cannot anticipate it. Reconsideration and withdrawal of the rejection are respectfully requested.

B. The rejection over Schiller et al.

The Examiner has next rejected claim 100 under 35 U.S.C. § 102(e) as allegedly being anticipated by Schiller *et al.,* U.S. Published Patent Application No. 2002/0081295. *See* Office Action at pages 5-6. Applicants respectfully traverse this rejection.

In order to expedite prosecution, and not in acquiescence to Examiner's rejection, Applicants have amended claim 100 to incorporate elements from dependant claims 103 and 121. As claims 103 and 121 were not rejected over Schiller *et al.*, Applicants presume that the Examiner has determined that these claims are allowable over this reference. Since the subject matter of these claims has now been incorporated into claim 100, Applicants respectfully contend that claim 100 is now allowable.

Nevertheless, Schiller *et al.* do not disclose the presently claimed invention. The reference discloses a mouse TNF-α arrayed on a papilloma-VLP, and does not disclose and/or enable the presently claimed compositions. Accordingly, Schiller *et al.* do not do not anticipate the presently claimed invention. Reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(e) are respectfully requested.

VIII. Rejections Under 35 U.S.C. § 103

The Examiner has next rejected claim 100 under 35 U.S.C. § 103(a) as allegedly being obvious over the combined teachings of Chackerian *et al.* and Renner *et al.* Applicants respectfully traverse this rejection.

The Examiner bears the burden of establishing a *prima facie* case of obviousness based upon the prior art. *See In re Piasecki*, 223 USPQ 785, 787-88 (Fed. Cir. 1984). The Examiner can satisfy this burden only by showing some objective teaching in the prior art, or that knowledge generally available to one of ordinary skill in the art, would lead that individual to combine the relevant teachings of the references in such a way as to produce the invention as claimed. *See In re Fine*, 5 USPQ2d 1596,1598 (Fed. Cir. 1988).

In the Office Action at page 7, the Examiner states that:

> (It) would have been within the ordinary skill in the art to modify the teachings of Chackerian by using the alternative links taught by Renner *et al.*, and it would have been within the ordinary skill of the art to modify the teachings Renner by choosing a self antigen for presentation as taught by Chackerian, with reasonable expectation of success.

Applicants respectfully disagree with these statements. Chackerian *et al.* provide no reason, suggestion or motivation to modify the linkages between the virus-like particle and the antigen. Similarly, Chackerian *et al.* provide no reason, suggestion or motivation to use alternative molecular scaffolds. Moreover, the Examiner has pointed to no other objective evidence to support the contention that modifying Renner with Chackerian was "within the ordinary skill of the art." Absent a reason, suggestion or motivation, other objective evidence, or sound scientific reasoning, the references cannot properly be combined. *See. Fine*, 5 USPQ2d at 1598. For at least the foregoing reasons, the Examiner has not met the burden of establishing a *prima facie* case of obviousness. Hence, Applicants respectfully

assert that the presently claimed invention would not have been obvious over the cited references. Applicants respectfully request reconsideration and withdrawal of the rejection.

IX. Other Matters

Applicants note that the Examiner has acknowledged that the elected combination is free of the art, and that the claims would be allowable if limited to the elected species. Applicants request that the Examiner allow the claims to the elected species, including the generic linking claims, and thereafter examine and allow claims to the nonelected species that are linked by such allowable linking claims, in accordance with MPEP § 809.04.

An initialed copy of Form PTO-1449 was appended to the Examiner's Office Action. The Examiner has noted that document AS95 could not be found. Applicants enclose herewith a courtesy copy of the document. Consideration of Document No. AS95 and an indication thereof on the record are respectfully requested.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided. Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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(54) Title: ORDERED MOLECULAR PRESENTATION OF ANTIGENS, METHOD OF PREPARATION AND USE

(57) Abstract

The invention provides compositions and processes for the production of ordered and repetitive antigen or antigenic determinant arrays. The compositions of the invention are useful for the production of vaccines for the prevention of infectious diseases, the treatment of allergies and the treatment of cancers. Various embodiments of the invention provide for a virus, virus–like particle, viral capsid particle, phage or recombinant form thereof coated with any desired antigen in a highly ordered and repetitive fashion as the result of specific interactions. In one specific embodiment, a versatile new technology based on a cassette–type system (Alpha Vaccine Technology) allows production of antigen coated viral particles. Other specific embodiments allow the production of antigen coated hepatitis B virus–like particles or antigen coated Measles virus–like particles.

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INTERNATIONAL SEARCH REPORT

Interna al Application No
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A. CLASSIFICATION OF SUBJECT MATTER
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B. FIELDS SEARCHED

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IPC 7 A61K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	ESPOSITO, GENNARO (1) ET AL: "Conformational study of a short pertussis toxin T cell epitope incorporated in a multiple antigen peptide template by CD and two-dimensional NMR: Analysis of the structural effects on the activity o synthetic immunogens." EUROPEAN JOURNAL OF BIOCHEMISTRY, (1993) VOL. 217, NO. 1, PP. 171-187. , XP000910191 the whole document --- -/--	1-30, 34-49

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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Interna al Application No
PCT/IB 99/01925

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	BACHMANN M F ET AL: "The influence of virus structure on antibody responses and virus serotype formation." IMMUNOLOGY TODAY, (1996 DEC) 17 (12) 553-8. REF: 48 , XP004071007 cited in the application the whole document	1-30, 34-49
A	WO 94 15585 A (UNIV CALIFORNIA) 21 July 1994 (1994-07-21) page 6 -page 12	1-30, 34-49
A	FROLOV, ILYA ET AL: "Alphavirus -based expression vectors: Strategies and applications" PROC. NATL. ACAD. SCI. U. S. A. (1996), 93(21), 11371-11377 , XP000910193 the whole document	31-33
T	BOORSMA M ET AL: "A temperature-regulated replicon-based DNA expression system." NATURE BIOTECHNOLOGY, (2000 APR) 18 (4) 429-32. , XP000910192 the whole document	31-33

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB 99/01925

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 35-40 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Internal Application No
PCT/IB 99/01925

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9415585 A	21-07-1994	US 5334394 A	02-08-1994
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